

3D-Transesophageal Echocardiography in Paradoxical Low-Flow, Low-Gradient Aortic Stenosis

Eco 3D transesofágico en la estenosis aórtica con bajo flujo/bajo gradiente paradójico

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ABSTRACT

Background: In paradoxical low-flow, low gradient (LF-LG) aortic stenosis, 2D-transthoracic echocardiography (2D-TTE) may underestimate flow because it assumes a circular left ventricular outflow tract (LVOT) shape. Three-dimensional transesophageal echocardiography (3D-TEE) is a better method to measure LVOT area.

Objectives: The aim of this study was to evaluate left ventricular stroke volume index (SVi) by 2D-TTE and 3D-TEE in patients with normal heart (NG) and with severe aortic stenosis (ASG) and to determine how many patients are categorized as paradoxical LF-LG by 2D-TTE and 3D-TEE.

Methods: Thirty-five patients were evaluated by 2D-TEE and 3D-TEE: NG=17 patients and ASG=18 patients. Left ventricular outflow tract area was estimated during early systole (ES) by 2D-TTE (ES2DLVOT Ar) and by 3D-TEE (ES3DLVOT Ar) planimetry, and as systolic average (Avg 3DLVOT Ar). Each LVOT area was multiplied by its corresponding flow integral to obtain SVi (ES2D-TTE SVi, ES3D-TTE SVi and Avg 3D-TTE SVi) in NG and ASG. Paradoxical LF-LG was determined in ASG following standard criterion.

Results: NG: ES2DLVOT Ar vs. ES3DLVOT Ar $p < 0.05$; ASG: ES2DLVOT Ar vs. ES3DLVOT Ar $p < 0.001$ and vs. Avg 3DLVOT Ar $p < 0.023$; ES2D-TTE SVi vs. ES3D-TTE SVi $p < 0.002$ and vs. Avg 3D-TTE SVi $p < 0.038$. In the NG, the lower limit of normal SVi for 2D-TTE, ES3D-TTE and Avg 3D-TTE was < 34 , < 38.9 and < 35.9 ml/m², respectively. Three patients with severe aortic stenosis were categorized as paradoxical LF-LG by 2D-TTE, but none by 3D-TEE.

Conclusions: Patients with paradoxical LF-LG by 2D-TTE could be recategorized by 3D-TEE. This finding is related with the limitations of 2D-echocardiography for estimating LVOT area.

Key words: Aortic Valve Stenosis/Pathophysiology - Aortic Valve/Ultrasonography - Echocardiography, Transesophageal - Echocardiography, Three-Dimensional - Blood Flow Velocity

RESUMEN

Introducción: En la estenosis aórtica (EAo) con bajo flujo/bajo gradiente paradójico (BFBGP), el eco transtorácico 2D (ETT2D) podría subestimar el cálculo de flujo porque asume el tracto de salida del ventrículo izquierdo (TSVI) con una morfología circular. El eco transesofágico 3D (ETE3D) es metodológicamente mejor que el 2D para medir el TSVI.

Objetivos: Evaluar el volumen eyectivo indexado (VEi) del ventrículo izquierdo por ETT2D y ETE3D en pacientes con corazón normal (GN) y con EAo grave (GEAo) y determinar cuántos pacientes con BFBGP por ETT2D se consideran también con BFBGP por ETE3D.

Material y métodos: Se evaluaron 35 pacientes con ETT2D y ETE3D: GN = 17 pacientes y GEAo = 18 pacientes. Se estimó en ambos grupos el área del TSVI en protosístole por ETT2D (TSVI2Dprot) y por planimetría ETE3D (TSVI3Dprot) y como promedio sistólico (TSVI3Dprom). Multiplicando cada área del TSVI por su integral de flujo, se obtuvieron los VEi (VEi ETT2D prot, VEi ETE3D prot y VEi ETE3D prom) tanto del GN como del GEAo. En el GEAo se determinó BFBGP según criterio actual.

Resultados: GN: área TSVI ETT2D protvs. ETE3D prot $p < 0,05$. GEAo: área TSVI ETT2D protvs. ETE3D prot $p < 0,001$ y vs. ETE3D prom $p < 0,023$; VEi ETT2D protvs. VEi ETE3D prot $p < 0,002$ y vs. VEi ETE3D prom $p < 0,038$. En el GN, el VEi en el límite inferior de lo normal por ETT2D, ETE3D prot y ETE3D prom fue < 34 , $< 38,9$ y $< 35,9$ ml/m², respectivamente. Tres pacientes del GEAo fueron BFBGP por ETT2D, pero ninguno por ETE3D.

Conclusiones: Los pacientes con BFBGP por ETT2D podrían ser reclasificados por el ETE3D. Este hallazgo se relaciona con las limitaciones del eco 2D para el cálculo del área del TSVI.

Palabras clave: Estenosis de la válvula aórtica/Fisiopatología - Válvula aórtica/Ultrasonografía - Ecocardiografía transesofágica - Ecocardiografía tridimensional - Velocidad de flujo sanguíneo

REV ARGENT CARDIOL 2015;83:326-333. <http://dx.doi.org/10.7775/rac.v83.i4.5689>

SEE RELATED ARTICLE: Rev Argent Cardiol 2014;82:279-281. <http://dx.doi.org/10.7775/rac.v83.i4.6729>

Received: 01/27/2015 - Accepted: 03/27/2015

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Abbreviations

AVA	Aortic valve area	NG	Normal group
LF-LG	Low-flow, low-gradient	NF-LG	Normal-flow, low-gradient
AS	Aortic stenosis	Avg	Average
2D-TEE	Two-dimensional transesophageal echocardiography	ES	Early systole
3D-TEE	Three-dimensional transesophageal echocardiography	LVOT	Left ventricular outflow tract.
2D-TTE	Two-dimensional transthoracic echocardiography	SVi	Stroke volume index
EF	Ejection fraction	VTI	Velocity time integral
ASG	Aortic stenosis group		

INTRODUCTION

The incidence of aortic stenosis (AS) is continuously increasing due to progressive growth of the elderly population. (1) The parameters referred to for the grading of aortic valve stenosis severity, based on data obtained from two-dimensional transthoracic echocardiography (2D-TTE), are aortic valve area (AVA) $<1 \text{ cm}^2$ or AVA index $<0.6 \text{ cm}^2/\text{m}^2$ and mean pressure gradient $>40 \text{ mmHg}$. (2) In daily practice, measurement of AVA using the continuity equation obtained by 2D-TTE is commonly associated with discrepancies between AVA and the pressure gradient: AVA $<1 \text{ cm}^2$ with mean pressure $<40 \text{ mmHg}$, which is easy to understand in patients with low ejection fraction (EF) but becomes difficult to explain when the EF is normal. (3) Hachicha et al. (4) described a subgroup of patients with AS and preserved EF ($>50\%$) in whom the inconsistent grading was not such, but was rather a low-flow pattern with stroke volume index (SVi) $\leq 35 \text{ ml/m}^2$. This pattern was associated with smaller left ventricular cavity and a greater degree of concentric remodeling, lower stroke volume, excessive afterload, and reduced myocardial contractility despite normal ejection fraction. This entity was called low-flow, low-gradient (LF-LG) AS with preserved left ventricular function or paradoxical low-flow, low-gradient. One of the questionings about this new entity is the hypothesis of probable errors in measuring the left ventricular outflow tract (LVOT) diameter. (5) Three-dimensional transesophageal echocardiography (3D-TEE) is an excellent tool to measure LVOT without assuming its geometry and could unmask a wrong diagnosis of paradoxical LF-LG AS. It would be necessary to know the normal values of SVi measured by 2D-TTE and 3D-TEE in a group of subjects without structural heart disease and to determine which value corresponds to low flow.

The goals of this study were: 1) to determine left ventricular SVi by 2D-TTE and 3D-TEE in patients with structurally normal hearts, and, 2) to determine how many patients with severe AS are categorized as paradoxical LF-LG by both 2D-TTE and 3D-TEE.

METHODS

The study has a cross-sectional design. Patients were consecutively and prospectively included in two groups: one control group with structurally normal heart (NG) and an-

other group of patients with severe aortic stenosis (ASG). A total of 17 patients (46 ± 16 years old; 10 women) with indication of transesophageal echocardiography (in 13 patients to evaluate cardioembolic source and in 4 patients due to febrile syndrome) were included. All patients had normal 2D-TTE, were in sinus rhythm and had blood pressure $<130/90 \text{ mmHg}$. Patients with arrhythmias that could affect parameter determinations were excluded.

The ASG consisted of 18 patients (73.5 ± 9 years old; 12 men) in sinus rhythm, with an AVA index $<0.6 \text{ cm}^2/\text{m}^2$ measured by the continuity equation with 2D-TTE. Paradoxical LF-LG AS was determined in the subgroup of patients with SVi in 2D-TTE $<35 \text{ ml/m}^2$, mean pressure gradient $<40 \text{ mmHg}$ and left ventricular EF $>50\%$.

Echocardiography protocol

Both groups underwent 2D-TTE, 2D-TEE and 3D-TEE with a Philips iE33 3D echocardiographic imaging platform (Philips Ultrasound USA), capable of acquiring 2D digital images, 3D real-time (live) images and full volume gated images. This complete 3D capture was transferred to a workstation and then analyzed using QLAB 8.1 software (Philips Medical System). Firstly, 2D-TTE was performed according to the usual protocol. Immediately after, an X7-2t multiplanar transesophageal probe was introduced under sedation administered by an anesthesiologist, and TEE was performed. Full volumes were acquired in 3-chamber view with visualization of the aortic root and descending aorta at 135° degrees of 2D-TEE. The best 3D capture without stitching artifacts was chosen. All the measurements were performed by a single experienced operator trained in the management of the QLAB software. Each determination was measured three times and an average value was obtained to reduce intra observer variability.

Stroke volume index was estimated in both groups multiplying LVOT area (in cm^2) by LVOT velocity time integral (VTI) (cm) calculated by pulsed Doppler echocardiography. LVOT VTI was estimated in 2D-TTE before performing TEE and during TEE (under intravenous sedation), changing the probe to 2D-TTE after obtaining a correct 3D acquisition in the 3-chamber view. LVOT area by 2D-TTE was estimated with the usual method using LVOT diameter in early systole (ES2DLVOT Ar) according to the usual formula: $\pi \cdot (\text{diameter}/2)^2$ (Figure 1 A). LVOT area by 3D-TEE was obtained by direct planimetry at 5 mm of the aortic annulus in early systole (ES3DLVOT Ar) and as the average area in each systolic frame (Avg 3DLVOT Ar) (Figure 1 B). Each LVOT area (ES2DLVOT Ar, ES3DLVOT Ar and Avg 3DLVOT Ar) was multiplied by its corresponding VTI and during each technique (2D-TTE and 3D-TEE) to obtain stroke volume indexes: 2D SVi in early systole, 3D-SVi in early systole and average 3D-SVi in the NG and ASG. Volume

measurements by 3D-TEE is a hybrid 2D/3D approach that combines 2D transthoracic Doppler echocardiography with LVOT planimetry by 3D-TEE (Figure 1 C), with simultaneous measurement and similar hemodynamic variables (with the patient sedated and monitored by an anesthesiologist). The effective orifice area is then calculated by dividing this stroke volume by the aortic valve VTI with continuous Doppler, with LVOT corrected by 3D-TEE (effective AVA measured by hybrid 2D/3D approach). The SVi obtained in the group of normal patients was used to determine how many paradoxical LF-LG patients by 2D-TTE were also considered as paradoxical LF-LG by 3D-TEE. We did not compare LVOT area by 2D-TTE because the method has the same limitations of 2D-TTE (it also assumes a circular LVOT shape).

Statistical analysis

Quantitative variables are expressed as mean $\pm$ standard deviation. Qualitative variables are presented as percentages. The Mann-Whitney test was used to compare two quantitative variables. In case of multiple comparisons, nonparametric methods (Kruskal-Wallis test) or ANOVA followed by Scheffé were used, as applicable. The Bland-Altman plot was used to estimate the concordance between the differ-

ent methods. In the NG, normal SVi was considered as the mean ± 2 standard deviations. A p value < 0.05 was considered statistically significant.

Ethical considerations

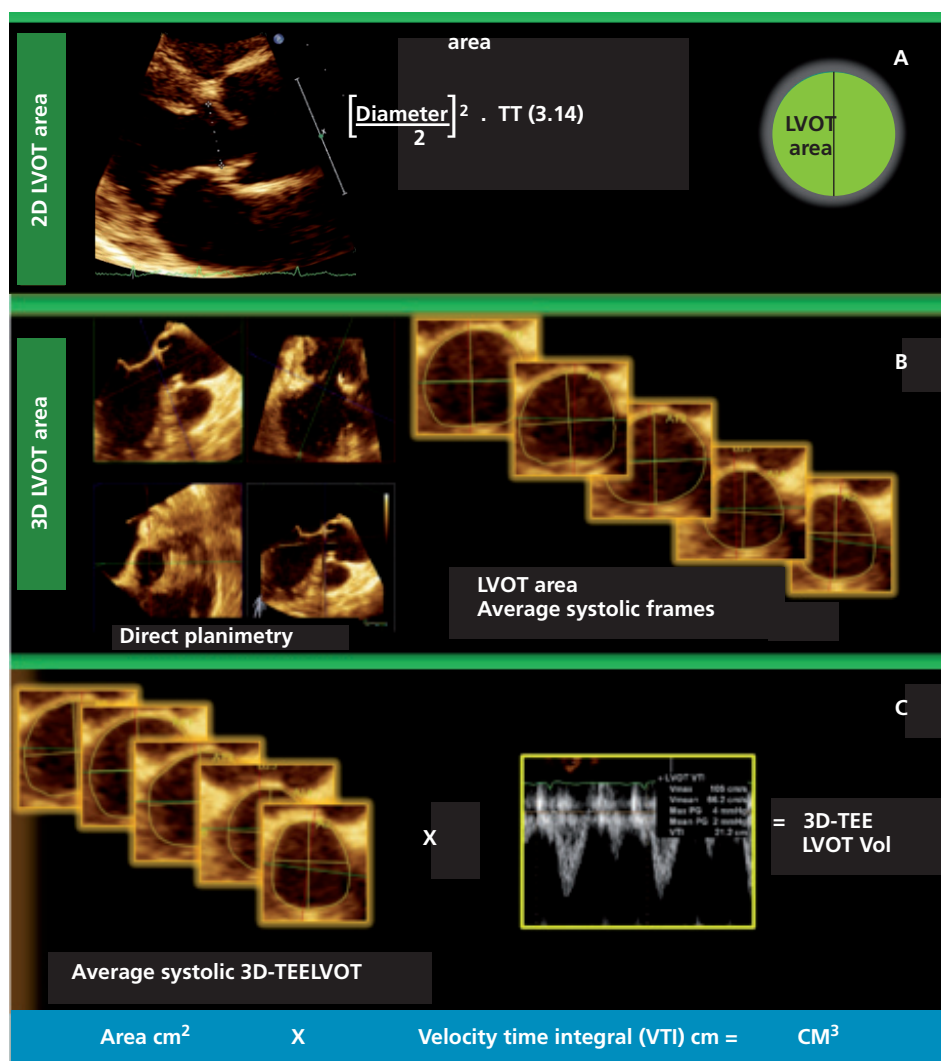
The protocol was evaluated and approved by the Institutional Review Board.

RESULTS

In the NG, LVOT VTI (cm) measured during 2D-TTE before performing 3D-TEE did not show significant differences with LVOT VTI measured by 2D-TTE during TEE (20.8 ± 2.02 vs. 20.3 ± 2.44). LVOT area measured by 3D-TEE in early systole was greater than the area measured by 2D-TTE in early systole ($p < 0.05$), but there were no differences between Avg 3DLVOT Ar vs. 2D-TTE in early systole and between Avg 3D-TEE vs. 3D-TEE in early systole. There were no differences between ES2D-TTESVi, ES3D-TEESVi and Avg 3D-TEESVi (Table 1).

In the ASG, AVA estimated by the continuity equation was $0.65 (\pm 0.24) \text{ cm}^2$ and the AVA index was

Fig. 1. A. Usual method to measure left ventricular outflow tract (LVOT) by 2D-TTE (it assumes a LVOT circular shape). **B.** Measurement of LVOT by 3D-TEE using direct planimetry after correct alignment of the 2D orthogonal planes and in each systolic frame. **C.** Hybrid 2D/3D approach to measure stroke volume multiplying average areas (frame by frame) of systole per time velocity integral by 2D-TTE.



Variable	NG n=17	mean 95% CI	ASG n=18	mean 95% CI	p
Age, years	46.7 (±16)	38-55.4	73.5 (±9)	68.8-78.1	< 0.001
Men, n (%)	10 (58.8)	34.9-79.9	12 (66)	43.0-85.2	ns
Bodysurfacearea, m ²	1.81 (±0.18)	1.72-1.90	1.85 (±0.23)	1.74-1.96	ns
LVEF, (%)	62.9 (±3.48)	61.2-64.5	52 (±13)	46.0-58.0	0.02
2D-TTELVOT diameter, cm	2.04 (±0.16)	1.96-2.12	1.99 (±0.2)	1.8-1.9	ns
2D-TTELVOT VTI	20.8 (±2.02)	19.7-21.8	20.3 (±5)	17.8-22.8	ns
2D-TTE during TEELVOT VTI	20.3 (±2.44)	18.9-21.6	20.6 (±5.7)	16.2-25.0	ns
ES2D-TTELVOT Ar, cm ²	3.29 (±0.5)	3.02-3.57	3.16 (±0.8)	2.75-3.57	ns
ES3D-TEELVOT Ar, cm ²	3.83 (±0.6)	3.51-4.15	4.04 (±0.7)	3.68-4.41	ns
Avg 3D-TEELVOT Ar, cm ²	3.54 (±0.6)	3.23-3.86	3.82 (±0.6)	3.49-4.15	ns
ES2D-TTESVi, ml/m ²	38.2 (±8.03)	34.0-42.3	34.04 (±8.6)	29.7-38.3	ns
ES3D-TEESVi, ml/m ²	43.4 (±8.6)	38.9-47.8	43.5 (±9.6)	38.7-48.3	ns
Avg 3D-TEESVi ml/m ²	40.1 (±8.3)	35.9-44.4	41.1 (±9.6)	36.3-45.9	ns

The number between brackets is the standard deviation. LVOT: Left ventricular outflow tract. VTI: Velocity time integral. 2D-TTE: Two-dimensional transthoracic echocardiography. 3D-TEE: Three-dimensional transesophageal echocardiography. ES: Early systole. SVI: Stroke volume index. Avg: average.

Table 1. Characteristics of the normal group and aortic stenosis group

0.35 (± 0.11) cm²/m², peak pressure gradient was 66 (± 19) mmHg and mean pressure gradient 41 (± 14) mmHg. Ejection fraction was 52% (± 13). LVOT VTI measured by 2D-TTE before 3D-TEE was 20.3 ± 5 and showed no significant differences with LVOT VTI measured by 2D-TTE during TEE (20.6 ± 5.7). Systolic blood pressure during 2D-TTE was 134 mmHg (± 16) vs. 120 mmHg (± 30) during 3D-TEE at the moment of measuring LVOT VTI (p = ns). There were significant differences in ES2DLVOT Ar (cm²) (3.16 ± 08) vs. ES3DLVOT Ar (4.04 ± 0.7) and ES2DLVOT Ar vs. Avg 3DLVOT Ar (3.82 ± 0.6) (p < 0.001 and p < 0.023, respectively) and no concordance (Table 2; Figure 3). There were no differences between ES3DLVOT Ar vs. Avg 3DLVOT Ar. ES2DSVi (ml/m²) vs. ES-3DSVi, and ES2DSVi vs. Avg 3DSVi showed statistically significant differences (p < 0.002 and p < 0.038, respectively) and no concordance (Table 2). LVOT diameters (cm) measured by 2D-TTE in the NG vs. ASG had no differences (2.04 vs. 1.99; p=ns).

In the NG, the lower limit of normal SVi taken as the cutoff value to consider low flow was <34 ml/m² by 2D-TTE and <38.9 ml/m² by 3D-TEE, measuring LVOT in early systole, and <35.9 ml/m² measuring the average LVOT with 3D-TEE during the entire systole.

Among the 18 patients in ASG, 3 (16%) had paradoxical LF-LG according to the usual definition (<35 ml/m², mean pressure gradient <40 mmHg and EF >50%) with ES2DSVi 30.9 ml/m², mean pressure gradient 27.6 mmHg and EF 54.6%. Two of these 3 patients had paradoxical LF-LG by 2D-TTE according to the cut-off value of our population (low flow <34 ml/m²). None of these three patients was categorized as paradoxical LF-LG considering the SVi by 3D-TEE, either measuring LVOT in early systole (40.2ml/m²) or

Table 2. Concordance between the methods

Variable	95% CI concordance	p
NG ES2D-TTELVOT Ar cm ² vs. ES3D-TEELVOT Ar cm ²	-1.75-1.25	<0.0001
ASG ES2D-TTELVOT Ar cm ² vs. Avg 3D-TEELVOT Ar cm ²	-2.08-1.58	<0.0001
ASG ES2D-TTELVOT Ar cm ² vs. ES3D-TEELVOT Ar cm ²	-2.32-1.798	<0.0001
ASG ES2D-TTESVi ml/m ² vs. ES3D-TEESVi, ml/m ²	-12.18-6.84	<0.0001
ASG ES2D-TTESVi ml/m ² vs. Avg 3D-TEESVi ml/m ²	-10.05-4.15	<0.0001

Method: Bland-Altman

NG: Normal group. ASG: Aortic stenosis group. LVOT: Left ventricular outflow tract. 2D-TTE: Two-dimensional transthoracic echocardiography. 3D-TEE: Three-dimensional transesophageal echocardiography. ES: Early systole. Avg: average. SVI: Stroke volume index.

the average LVOT throughout the entire systole (38.9 ml/m²) (Table 3)

DISCUSSION

The incidence of paradoxical LF-LG AS ranges between 9% and 35% in the published literature. (4, 6) Its prognosis and real incidence are controversial, and even its existence is questioned. (5) Some authors have reported an adverse long-term outcome, while others have found that the prognosis is similar to that of moderate AS. (7)

LVOT flow estimation, which depends on LVOT size, is the key for its diagnosis. (8) LVOT is oval rather than circular and its minimal diameter, measured

Fig. 2. Severe aortic stenosis in the same patient of Figure 1, but with different measurements of left ventricular outflow tract (LVOT) by 3D-TEE and from orthogonal planes. See how calcium complicates the measurement of the aortic valve area (A, down, to the left) and how the area varies with minimal and imperceptible changes in the position of the cursor (B, down, to the right).

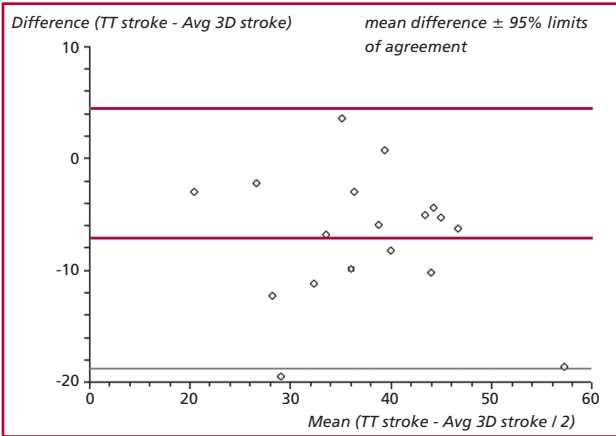
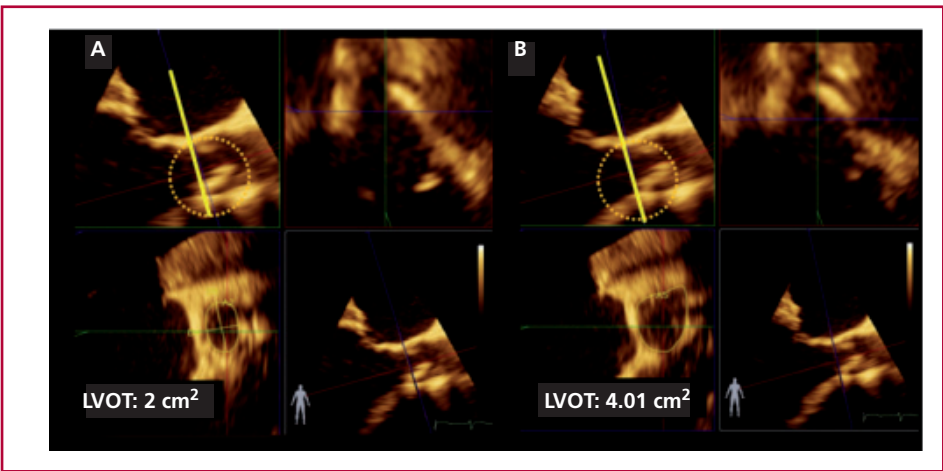


Fig. 3. Bland-Altman plot for the ASG: ES2D-TTESVi ml/m² vs. Avg 3D-TEESVi in systole ml/m². Limit of concordance 95%=10.05 to -4.15 ($p < 0.0001$). ASG: Aortic stenosis group. 2D-TTE: Two-dimensional transthoracic echocardiography. 3D-TEE: Three-dimensional transesophageal echocardiography. SVi: Stroke volume index.

by 2D-TTE, is antero-posterior. (9) A small measurement error in LVOT minimal diameter by 2D-TTE results in large errors in calculated values of stroke volume and AVA with the continuity equation. Hence, the 17% underestimated LVOT area on 2D versus 3D described in previous studies. (10) Left ventricular geometry associated with paradoxical LF-LG AS is common in elderly, hypertensive patients. Thus, it seems easy to overestimate this entity considering both conditions.

This study was designed to evaluate which patients categorized as paradoxical LF-LG AS by 2D-TTE did not have this condition when the stroke volume was measured by 3D-TEE using a cut-off value of low flow determined by 3D-TEE in normal subjects. We found that the 3 patients with the usual criteria of paradoxical LF-LG AS did not have low flow when SVi was measured by 3D-TEE using the cut-off value of SVi pre-established by 3D-TEE in the NG (< 38.9 ml/m²

Table 3. Characteristics of the 3 patients with paradoxical low-flow-low gradient aortic stenosis

	Patient 1	Patient 2	Patient 3
Sex	M	F	F
Age, years	84	54	72
Body surface area, m²	1.86	1.7	1.63
Mean pressure gradient, mmHg	31	23	29
Ejection fraction, %	50	59	55
ES2D-TTELVOT Ar, cm²	3.46	2	3.26
ES3D-TEELVOT Ar, cm²	4.97	3	3.58
Avg 3D-TEELVOT Ar, cm²	4.92	2.87	3.47
ES3D-TEESTU Ar, cm²	9.06	3.68	3.42
ES2D-TTESVi, ml/m²	31.1	26.8	34.9
ES3D-TEESVi, ml/m²	41.4	40.2	39.22
Avg 3D-TEESVi ml/m²	41	38	37.9
AVA 2D-TTE, cm²	0.72	0.7	0.67
AVA hybrid 2D/3D, cm²	0.87	0.91	0.71
AVAi 2D-TTE, cm²/m²	0.38	0.41	0.41
AVAi hybrid 2D/3D, cm²/m²	0.46	0.53	0.43

2D-TTE: Two-dimensional transthoracic echocardiography. 3D-TEE: Three-dimensional transesophageal echocardiography. ES: Early systole. Avg: average. STU: Sinotubular junction. SVi: Stroke volume index. AVA: Aortic valve area. i: index.

in early systole and < 35.9 ml/m² as systolic average). However, although effective AVA was greater in these 3 patients when it was measured by a hybrid 2D/3D approach, it was still < 1 cm² and < 0.6 cm²/m² (see Table 3). From paradoxical LF-LG, these patients were recategorized as AS < 1 cm² but with normal flow, low gradient (NF-LG) and preserved EF. This entity was described by Adda et al, (6) in a multicenter prospective study including 340 patients with AS, AVA < 1 cm² and preserved ejection fraction by 2D-TTE. They described that a larger number of patients (15%) pre-

sented with NF-LG, higher AVA, higher energy loss index, lower global afterload versus LF-LG patients (9%) and suggested that the probable error was measuring LVOT by 2D-TTE. Lancellotti et al. (11) demonstrated that patients with NF-LG had significantly lower natriuretic peptide than those with LF-LG.

Which are the probable reasons why none of the 3 patients with LF-LG by 2D-TTE were not also considered LF-LG by 3D-TEE?

The error of measuring LVOT by 2D-TTE. LVOT area was underestimated when it was measured by 2D-TTE versus 3D-TEE (our benchmark) in both NG and ASG. But underestimation was even greater in the ASG [the difference in LVOT area by 2D versus 3D in early systole in the ASG was 21.7% (0.88 cm²) and 13.7% in the NG (0.52 cm²)]. This finding can be explained by the fact that it is technically more difficult to measure LVOT diameter by 2D-echocardiography in the presence of calcific aortic valve disease (Figure 2). Then, the possibility of error is greater when the stroke volume is measured in the LVOT of a severe AS compared to LVOT without AS.

The probable error in the cut-off value to define low flow. The cut-off value to determine low flow in AS (SVi < 35 ml/m² by 2D-TTE) was obtained in an arbitrary fashion, based on the experience of previous studies, (4) without considering the limitation generated by calcium in the calculation of LVOT by 2D-TTE. However, defining a cut-off value of normal flow in a healthy population and then extrapolating it to an elderly population (ASG) may be controversial; but it may also be difficult to find an age group similar to that of ASG with normal 2D-TTE and indication of 2D/3D TEE and then evaluating which cut-off value would define normal flow in this population.

Is there error in the cut-off value for grading paradoxical LF-LG AS? The severity of aortic stenosis is determined by AVA and pressure gradient. Some authors proposed to lower the AVA cut-off value from 1 to 0.8 cm² because of the high rate of discrepancies observed between AVA and the pressure gradient measured by 2D-TTE, and because according to previous studies using the Gorlin formula an AVA of 1 cm² corresponds to a gradient of 26 mmHg. (5) If so, 2 of our 3 patients with paradoxical LF-LG would not have severe AS according to the SVi by 3D-TEE.

There are no studies in the literature with the same design as ours. González-Canovasy et al (13) evaluated 63 patients with paradoxical LF-LG AS using direct planimetry of the aortic valve by 3D-TEE and confirmed the presence of AVA < 1 cm² in 85% of cases and the existence of paradoxical LF-LG. But they analyzed LVOT flow only by 2D-TTE, without knowing in how many of these patients SVi defining paradoxical LF-LG could have been underestimated.

This study was not designed to reject the theory of paradoxical LF-LG, but questions which could be the cut-off value to define low flow in patients with AS and preserved EF. It also suggests that some pa-

tients considered as paradoxical LF-LG AS according to the current definition could be recategorized using 3D echocardiography techniques as NF-LG AS, which seems to be a more benign condition but with pathophysiology even more controversial than that of paradoxical LF-LG.

Study limitations

The number of patients in both groups (NG and ASG) is insufficient to reach conclusive results. Patients in the NG were younger, and the comparison between both groups could be a methodological error, particularly in terms of ventricular function and normal stroke volume. Although we interpreted 3D-TEE as the benchmark, 2D-TTE may underestimate and 3D-TEE may overestimate LVOT size due to the lack of a real reference standard. Interobserver variability was not analyzed.

CONCLUSIONS

In this population of patients with severe AS, the 3 patients with paradoxical LF-LG by 2D-TTE were recategorized as NF-LG by 3D-TEE. This finding is related to the limitations of 2D-echocardiography for estimating LVOT area, particularly in patients with calcific aortic valve disease. Further studies are needed in the same line of investigation to demonstrate whether 3D techniques can be useful to unmask paradoxical LF-LG AS diagnosed by 2D-echocardiography.

Conflicts of interest

None declared

(See author's conflicts of interest forms in the web / Supplementary Material)

REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart disease: a population-based study. *Lancet* 2006;368:1005-11. <http://doi.org/dhgzdrf>
2. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Valvular Heart Disease). *J Am Coll Cardiol* 2006;48:e1-148. <http://doi.org/b8q4ms>
3. Minners J, Allgeier M, Gohlke-Baerwolf C, Kienzle RP, Neumann FJ, Jander N. Inconsistencies of echocardiographic criteria for the grading of aortic valve stenosis. *Eur Heart J* 2008;29:1043-8. <http://doi.org/c8sczs>
4. Hachicha Z, Dumesnil JG, Bogaty P, Pibarot P. Paradoxical low-flow, low gradient severe aortic stenosis despite preserved ejection fraction is associated with higher afterload and reduced survival. *Circulation* 2007;115:2856-64. <http://doi.org/fgrqp7>
5. Jander N. Low-gradient 'severe' aortic stenosis with preserved ejection fraction: new entity, or discrepant definitions? *Eur Heart J* 2008;10 (SupplE):E11-5. <http://doi.org/fq2ss8>
6. Adda J, Mielot C, Giorgi R, Zirphile X, Donal E, Sportouch-Dukhan C, et al. Low-flow, low-gradient severe aortic stenosis despite normal ejection fraction is associated with severe left ventricular dysfunction as assessed by speckle-tracking echocardiography: a multicenter study. *Circ Cardiovasc Imaging* 2012;5:27-35. <http://doi.org/fdnmsh>
7. Jander N, Minners J, Holme I, Gerdtts E, Boman K, Brudi P, et al. Outcome of patients with low gradient "severe" aortic stenosis and

preserved ejection fraction. *Circulation* 2011;123:887-95. <http://doi.org/c2sgd9>

8. Michelena H, Margaryan E, Miller FA, Eleid M, Maalouf J, Suri R, et al. Inconsistent echocardiographic grading of aortic stenosis: is the left ventricular outflow tract important? *Heart* 2013;99:921-31. <http://doi.org/44n>

9. Falconi M, Funes D, Arias A, Bagnati R, Jaimovich G, Giacomini P et al. Assessment of Left Ventricular Outflow Tract Dynamics During the Cardiac Cycle by Three-Dimensional Echocardiography. *Rev Argent Cardiol* 2012;80:341-6. <http://doi.org/q3z>

10. Gaspar T, Adawi S, Sachner R, Asmer I, Ganaeem M, Rubinshtein R, et al. Three-dimensional imaging of the left ventricular outflow tract: impact on aortic valve area estimation by the continuity

equation. *J Am Soc Echocardiogr* 2012;25:749-57. <http://doi.org/44p11>

11. Lancellotti P, Magne J, Donal E, Davin L, O'Connor K, Rosca M, et al. Clinical Outcome in asymptomatic severe aortic stenosis insights from the new proposed aortic stenosis grading classification. *J Am Coll Cardiol* 2012;59:235-43. <http://doi.org/fzrdfc>

12. Gorlin R, Gorlin SG. Hydraulic formula for calculation of the area of the stenotic mitral valve, other cardiac valves, and central circulatory shunts. *Am Heart J* 1951;41:1-29. <http://doi.org/chkffm>

13. González-Canovas C, Muñoz-Esparza C, Oliva MJ, González-Carrillo J, López-Cuenca A, Gonzalo de la Morena et al. Severe aortic valve stenosis with low-gradient and preserved ejection fraction: a misclassification issue?. *Rev Esp Cardiol* 2013;66:255-60. <http://doi.org/f2ffk9>